PTO/SB/08a (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	10553532
Filing Date	2005-10-14
First Named Inventor	Mark S. Cushman et al.
Art Unit	1625
Examiner Name	Aulakh
Attorney Docket Number	3220-78751

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6509344		2003-01-21	Cushman et al.	
	2	5597831		1997-01-28	Michalsky et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	200021537	WO		2000-04-20			☐
	2	2004014862	WO		2004-02-19			☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10553532
	Filing Date	2005-10-14
	First Named Inventor	Mark S. Cushman et al.
	Art Unit	1625
	Examiner Name	Aulakh
	Attorney Docket Number	3220-78751

	3	03051289	WO		2003-06-26			☐
	4	2004014906	WO		2004-02-19			☐
	5	2004014918	WO		2004-02-19			☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	ANTONY et al., "Differential Induction of Topoisomerase I-DNA Cleavage Complexes by the Indenoisoquinoline MJ-III-65 (NSC 706744) and Camptothecin: Base Sequence Analysis and Activity Against Camptothecin-Resistant Topoisomerase I," Cancer Res., 2003, Vol. 63, pgs. 7428-7435	☐
	2	ANTONY et al., "Cellular Topoisomerase I Inhibition and Antiproliferative Activity by MJ-III-65 (NSC 706744), an Indenoisoquinoline Topoisomerase I Poison," Molecular Pharmacology, 2005, Vol. 67, No. 2, 523-530	☐
	3	CANAN KOCH et al., "Enantioselective Preparation of B-Alkyl-y-butyrolactones from Functionalized Ketene Dithioacetals," J. Org. Chem., 1993, Vol. 58, No. 10, 2725-2737	☐
	4	COREY et al., "A Total Synthesis of Natural 20(S)-Camptothecin," J. Org. Chem., Vol. 40, No. 14, 1975, pp. 2140-2141	☐
	5	CUSHMAN et al., "Stereoselective Oxidation by Thionyl Chloride Leading to the Indeno[1,2-c]isoquinoline System," J. Org. Chem., 1978, Vol. 43, No. 19, pgs. 3781-3783	☐
	6	CUSHMAN et al., "Synthesis and Antitumor Activity of Structural Analogues of the Anticancer Benzophenanthridine Alkaloid Fagaronine Chloride," J. Med. Chem., 1985, Vol. 28, No. 8, pp. 1031-1036	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10553532
	Filing Date	2005-10-14
	First Named Inventor	Mark S. Cushman et al.
	Art Unit	1625
	Examiner Name	Aulakh
	Attorney Docket Number	3220-78751

	7	CUSHMAN et al., "Synthesis and Biological Activity of Structural Analogues of the Anticancer Benzophenanthridine Alkaloid Nitidine Chloride," J. Med. Chem., 1984, Vol. 27, No. 4, 544-547	☐
	8	CUSHMAN et al., "Synthesis of New Indeno[1,2-c]isoquinolines: Cytotoxic Non-Camptothecin Topoisomerase I Inhibitors," J. Med. Chem., 2000, Vol. 43, No. 20, pgs. 3688-3698	☐
	9	CUSHMAN et al., "Total Synthesis of Nitidine Chloride," J. Org. Chem., 1978, Vol. 43, No. 2, pgs. 286-288	☐
	10	HERTZBERG et al., "On the Mechanism of Topoisomerase I Inhibition by Camptothecin: Evidence for Binding to an Enzyme-DNA Complex," Biochemistry, 1989, Vol. 28, No. 11, 4629-4638	☐
	11	HERTZBERG et al., "Modification of the Hydroxy Lactone Ring of Camptothecin: Inhibition of Mammalian Topoisomerase I and biological Activity," J. Med. Chem., 1989, Vol. 32, No. 3, 715-720	☐
	12	IOANOVICIU et al., "Synthesis and Mechanism of Action Studies of a Series of Norindenoisoquinoline Topoisomerase I Poisons Reveal an Inhibitor with a Flipped Orientation in the Ternary DNA-Enzyme-Inhibitor Complex As Determined by X-ray Crystallographic Analysis," J. Med. Chem., 2005, Vol. 48, No. 15, 4803-4814	☐
	13	JAYARAMAN et al., "Novel Oxidative Transformation of Indenoisoquinolines to Isoquinoline-3-spiro-3'-phthalides in the Presence of Osmium Tetraoxide and 4-methylmorpholine N-Oxide," J. Org. Chem., 1998, Vol. 63, No. 17, 5736-5737	☐
	14	JAYARAMAN et al., "Synthesis of New Dihydroindeno[1,2-c]isoquinoline and Indenoisoquinolinium Chloride Topoisomerase I Inhibitors Having High In Vivo Anticancer Activity in the Hollow Fiber Animal Model," J. Med. Chem., 2002, Vol. 45, No. 1, pgs. 242-249	☐
	15	KOHLHAGEN et al., "Protein-Linked DNA Strand Breaks Induced by NSC 314622, a Novel Noncamptothecin Topoisomerase I Poison," Mol. Pharmacol., 1998, Vol. 54, pgs. 50-58	☐
	16	KUBOVA et al., "Binding Properties of Nitidine and Its Indenoisoquinoline Analogue with DNA," Studia Biophs., 1986, Vol. 114, No. 1-3, pgs. 251-256	☐
	17	LI et al., "Synthesis of the Tricyclic ABC Ring Subunit of Mazamine A," Tetrahedron, Vol. 54 (1998), 6661-6676	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10553532
	Filing Date	2005-10-14
	First Named Inventor	Mark S. Cushman et al.
	Art Unit	1625
	Examiner Name	Aulakh
	Attorney Docket Number	3220-78751

	18	MORRELL et al., "Synthesis of nitrated indenoisoquinoles as topoisomerase I inhibitors," Bioorganic & Medicinal Chemistry Letters, Vol. 14 (2004), 3659-3663	☐
	19	NAGARAJAN et al., "Design, Synthesis, and Biological Evaluation of Indenoisoquinoline Topoisomerase I Inhibitors Featuring Polyamine Side Chains on the Lactam Nitrogen," J. Med. Chem., 2003, Vol. 46, No. 26, pgs. 5712-5724	☐
	20	NAGARAJAN et al., "Synthesis and Anticancer Activity of Simplified Indenoisoquinoline Topoisomerase I Inhibitors Lacking Substituents on the Aromatic Rings," J. Med. Chem., 2004, Vol. 47, No. 23, pgs. 5651-5661	☐
	21	PATEL et al., "Neuromuscular blocking activity of bis-4-benzyltetrahydroisoquinolinium esters in the cat," European Journal of Pharmaceutical Sciences , Vol. 4 (1996), 63-71	☐
	22	POMMIER et al, Editorial Overview " Topoisomerase Inhibitors: Why New Ones?", Opinion in Oncologic, Endocrine & Metabolic Investigational Drugs, 1(2), 168-169 (1999)	☐
	23	POMMIER et al., "Mechanism and action of eukaryotic DNA topoisomerase I and drugs targeted to the enzyme," Biochem. Biophys. Acta., 1400, 83-106 (1998)	☐
	24	POURQUIER et al., "Induction of Reversible Complexes between Eukaryotic DNA Topoisomerase I and DNA-containing Oxidative Base Damages," The Journal of Biological Chemistry, Vol. 274, No. 13, 1999, pp. 8516-8523	☐
	25	SHETTY et al., "Aromatic -Stacking in Solution as Revealed through the Aggregation of Phenylacetylene Macrocycles," J. Am. Chem. Soc., 1996, Vol. 118, No. 5, pgs. 1019-1027	☐
	26	SOMEKAWA et al., "Intramolecular [2+2]Photocycloadditions of 1-(w-Alkenyl)-2-pyridones Possessing an Ester Group on the Olefinic Carbon Chain," J. Org. Chem., 1992, Vol. 57, No. 21, 5708-5712	☐
	27	STAKER et al., "Structures of Three Classes of Anticancer Agents Bound to the Human Topoisomerase I-DNA Covalent Complex," J. Med. Chem., 2005, Vol. 48, No. 7, 2336-2345.	☐
	28	STAKER et al., "The Mechanism of Topoisomerase I Poisoning by a Camptothecin Analog," Proc. Natl. Acad. Sci. U. S.A., 2002, Vol. 99, No. 24, pgs. 15387-15392	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10553532
	Filing Date	2005-10-14
	First Named Inventor	Mark S. Cushman et al.
	Art Unit	1625
	Examiner Name	Aulakh
	Attorney Docket Number	3220-78751

	29	STRUMBERG et al., "Synthesis of Cytotoxic Indenoisoquinoline Topoisomerase I Poisons," J. Med. Chem., 1999, Vol. 42, No.3, pgs. 446-457	☐
	30	VANCE et al., "Structural Features of Nitroaromatics That Determine Mutagenic Activity in Salmonella typhimurium," Environmental Mutagenesis, 1984, Vol. 6, pgs. 797-811	☐
	31	WANG et al., "Differential Effects of Camptothecin Derivatives on Topoisomerase I-Mediated DNA Structure Modification," Biochemistry, 1998, Vol. 37, No. 26, 9399-9408	☐
	32	WANG et al., "Role of the 20-Hydroxyl Group in Camptothecin Binding by the Topoisomerase I-DNA Binary Complex," Biochemistry, 1999, Vol. 38, No. 14, 4374-4381	☐
	33	WAWZONEK et al., "The Synthesis and Reactions of 1-Carbamyl-11-ketoindeno[1,2-c]isoquinoline," J. Org. Chem., 1966, Vol. 31, pp. 1004-1006	☐
	34	WHITMORE et al., "The Preparation of Homophthalyl Cyclic Hydrazide and 4-Aminohomophthalyl Cyclic Hydrazide," J. Am. Chem. Soc., 1944, Vol. 66, pgs. 1237-1240	☐
	35	XIAO et al., "Design, synthesis, and biological evaluation of cytotoxic 11-aminoalkenylindenoisoquinoline and 11-diaminoalkenylindenoisoquinoline topoisomerase I inhibitors," Bioorganic & Medicinal Chemistry, Vol. 12 (2004), 5147-5160	☐
	36	XIAO et al., "Dihydroindenoisoquinolines function as prodrugs of indenoisoquinolines," Bioorganic & Medicinal Chemistry Letters, Vol. 15 (2005), 2795-2798	☐
	37	XIAO et al., "Novel Autoxidative Cleavage Reaction of 9-Fluoredenes Discovered during Synthesis of a Potential DNA-Threading Indenoisoquinoline," J. Org. Chem., 2004, Vol. 69, No. 22, 7495-7501	☐
	38	XIAO et al., "On the Binding of Indeno[1,2-c]isoquinolines in the DNA-Topoisomerase I Cleavage Complex," J. Med. Chem., 2005, Vol. 48, No. 9, 3231-3238	☐
	39		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10553532
	Filing Date	2005-10-14
	First Named Inventor	Mark S. Cushman et al.
	Art Unit	1625
	Examiner Name	Aulakh
	Attorney Docket Number	3220-78751

	40		☐
	41		☐
	42		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	10553532
Filing Date	2005-10-14
First Named Inventor	Mark S. Cushman et al.
Art Unit	1625
Examiner Name	Aulakh
Attorney Docket Number	3220-78751

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/jkb/	Date (YYYY-MM-DD)	2006-10-30
Name/Print	James K. Blodgett	Registration Number	48480

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.